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=> d his

     (FILE 'REGISTRY' ENTERED AT 12:44:52 ON 29 OCT 2001)
                DEL HIS Y
L1              STR 35849-47-9
L2            0 S L1
L3            5 S L1 FUL
                SAVE L3 TEMP UPPA2/A

     FILE 'HCAPLUS' ENTERED AT 12:51:49 ON 29 OCT 2001
L4            7 S L3

     FILE 'HCAOLD' ENTERED AT 12:52:17 ON 29 OCT 2001
L5            0 S L3
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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES:    28 OCT 2001  HIGHEST RN 365210-66-8
DICTIONARY FILE UPDATES:   28 OCT 2001  HIGHEST RN 365210-66-8

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER see
HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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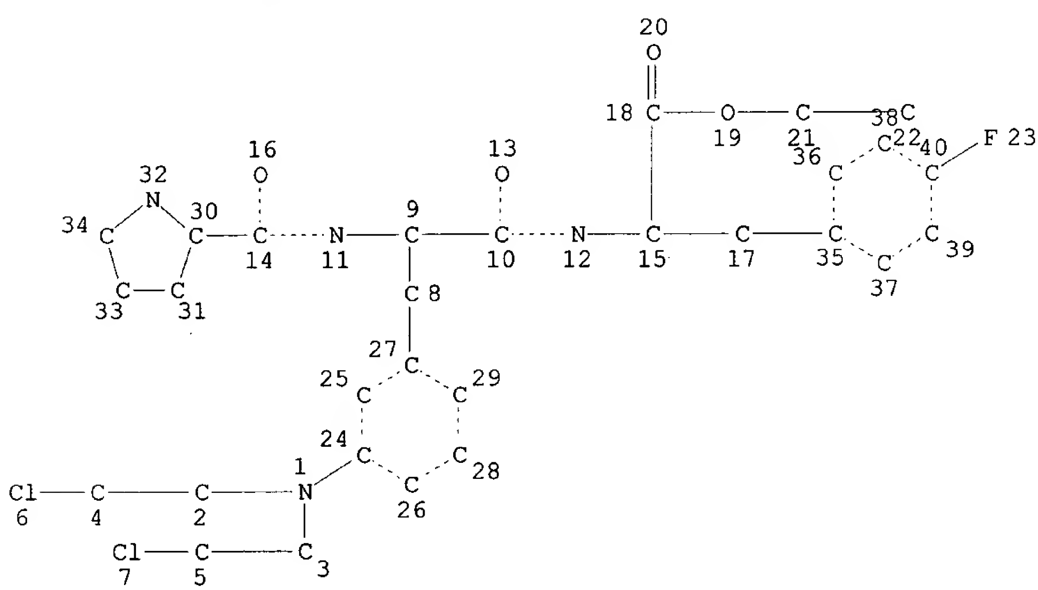

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  40

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED     19 ITERATIONS                        5 ANSWERS
SEARCH TIME: 00.00.01
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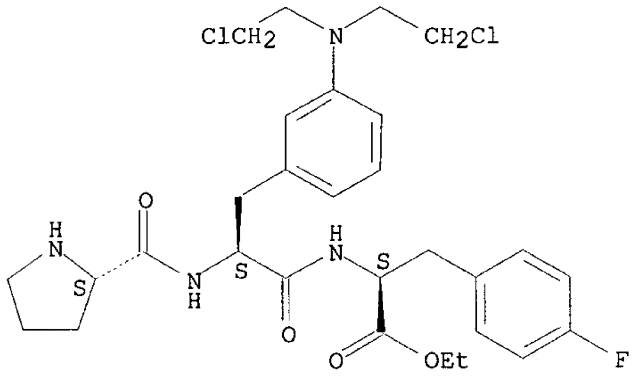
L3 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN 52237-41-9 REGISTRY
CN L-Phenylalanine, N-[3-[bis(2-chloroethyl)amino]-N-L-prolyl-L-phenylalanyl]-4-fluoro-, ethyl ester, monoacetate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H37 Cl2 F N4 O4 . C2 H4 O2
LC STN Files: CA, CAPLUS, TOXLIT

CM 1

CRN 52237-40-8
CMF C29 H37 Cl2 F N4 O4

Absolute stereochemistry. Rotation (-).



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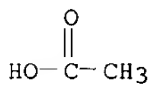
CRN 64-19-7
CMF C2 H4 O2

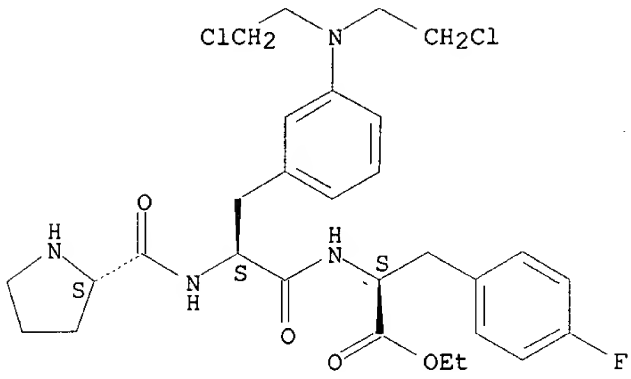


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 81:58145

L3 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN 52237-40-8 REGISTRY
CN L-Phenylalanine, L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Phenylalanine, N-[3-[bis(2-chloroethyl)amino]-N-L-prolyl-L-phenylalanyl]-4-fluoro-, ethyl ester
FS STEREOSEARCH
MF C29 H37 Cl2 F N4 O4
CI COM
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

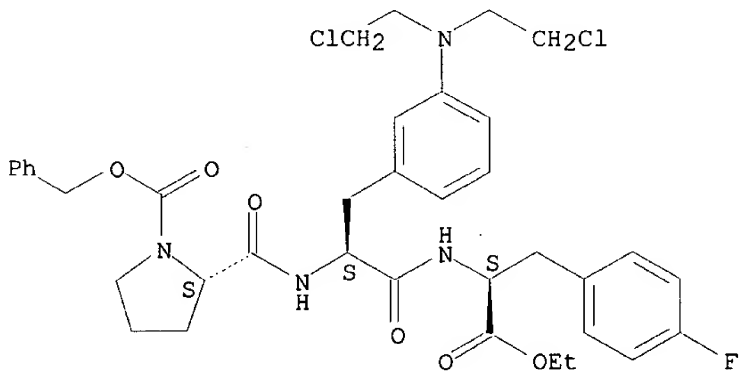
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:144179

REFERENCE 2: 129:285656

L3 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN 39064-36-3 REGISTRY
CN L-Phenylalanine, 1-[(phenylmethoxy)carbonyl]-L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Phenylalanine, N-[3-[bis(2-chloroethyl)amino]-N-[1-[(phenylmethoxy)carbonyl]-L-prolyl]-L-phenylalanyl]-4-fluoro-, ethyl ester
FS STEREOSEARCH
MF C37 H43 Cl2 F N4 O6
LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXLIT

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:347949

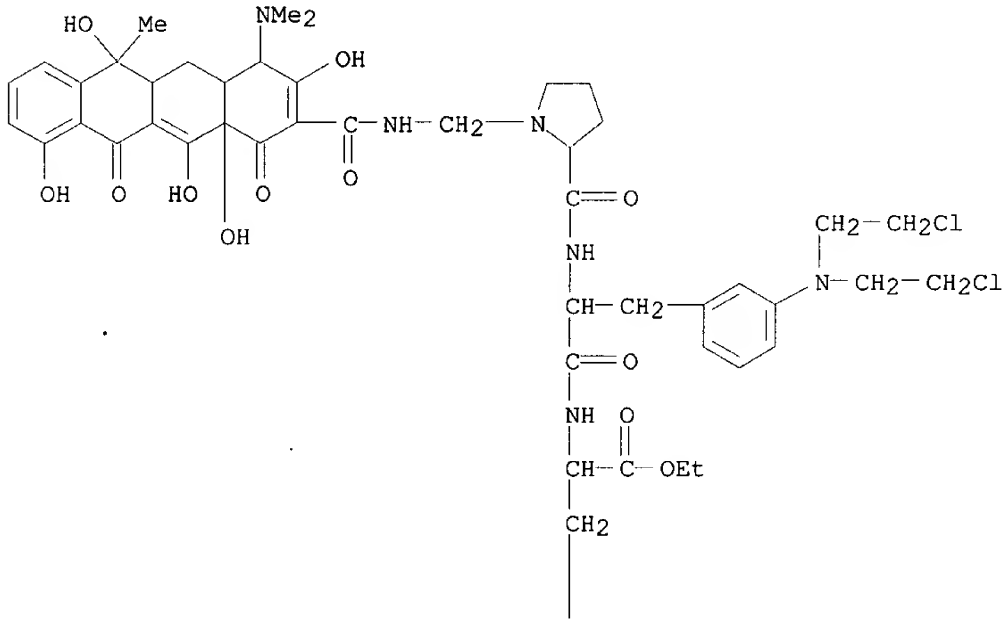
REFERENCE 2: 130:144179

REFERENCE 3: 78:72600

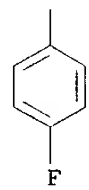
REFERENCE 4: 78:30201

L3 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN 39064-35-2 REGISTRY
CN L-Phenylalanine, N-[3-[bis(2-chloroethyl)amino]-N-[1-[[[[4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenyl]carbonyl]amino]methyl]-L-prolyl]-L-phenylalanyl]-4-fluoro-, ethyl ester, monohydrochloride, [4S-(4.alpha.,4a.alpha.,5a.alpha.,6.beta.,12a.alpha.)]- (9CI) (CA INDEX NAME)
MF C52 H61 Cl2 F N6 O12 . Cl H
LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB

PAGE 1-A



PAGE 2-A



HCl

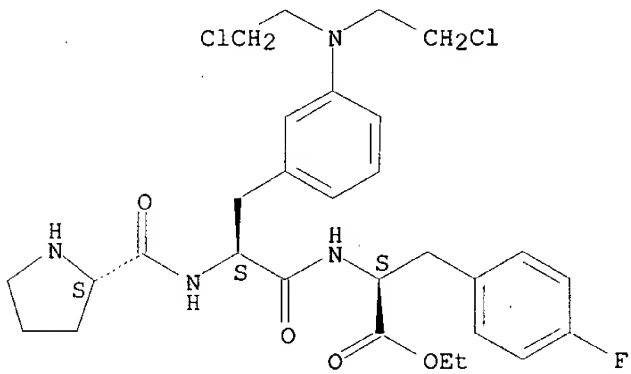
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 78:72600

REFERENCE 2: 78:30201

L3 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN 35849-47-9 REGISTRY
CN L-Phenylalanine, L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Phenylalanine, N-[3-[bis(2-chloroethyl)amino]-N-L-prolyl-L-phenylalanyl]-4-fluoro-, ethyl ester, monohydrochloride
FS STEREOSEARCH
MF C29 H37 Cl2 F N4 O4 . Cl H
LC STN Files: CA, CAPLUS, CASREACT, CHEMLIST, IFICDB, IFIPAT, IFIUDB, TOXLIT
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (52237-40-8)

Absolute stereochemistry. Rotation (-).



● HCl

5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:347949

REFERENCE 2: 130:144179

REFERENCE 3: 78:72600

REFERENCE 4: 78:30201

REFERENCE 5: 76:86148

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 12:52:46 ON 29 OCT 2001

FILE COVERS 1947 - 29 Oct 2001 VOL 135 ISS 19
FILE LAST UPDATED: 28 Oct 2001 (20011028/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d his l4

(FILE 'REGISTRY' ENTERED AT 12:44:52 ON 29 OCT 2001)
SAVE L3 TEMP UPPA2/A

FILE 'HCAPLUS' ENTERED AT 12:51:49 ON 29 OCT 2001
L4 7 S L3

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'.CA HITSTR L1-999 ' IS NOT A VALID STRUCTURE FORMAT KEYWORD
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=> d .ca hitstr l4 1-7

L4 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:368410 HCAPLUS
DOCUMENT NUMBER: 132:347949
TITLE: Method for producing L-prolyl-L-m-sarcolysyl-L-p-fluorophenylalanine and derivatives thereof
INVENTOR(S): Mehlem, Francesco; Di Vittorio, Pietro
PATENT ASSIGNEE(S): Peptichemio A.-G., Switz.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

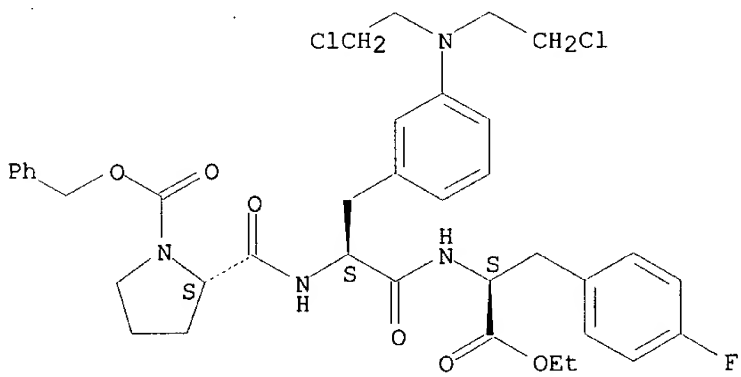
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000031119	A1	20000602	WO 1998-CH498	19981119
W: AU, CA, HU, IL, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9910193	A1	20000613	AU 1999-10193	19981119

EP 1129107 A1 20010905 EP 1998-952496 19981119
R: AT, BE, ES, NL, SE
PRIORITY APPLN. INFO.: WO 1998-CH498 A 19981119
OTHER SOURCE(S): CASREACT 132:347949; MARPAT 132:347949

AB An improved synthesis of the title compd., a component of the chemotherapeutic mixt. Peptichemio, and its alkyl esters or acid addn. salts, is claimed. Thus, C-terminal protected L-p-fluorophenylalanine was reacted with N-protected L-m-sarcolysine in the presence of dicyclohexylcarbodiimide, to give N,C-protected L-m-sarcolysyl-L-p-fluorophenylalanine. The N-protecting group was removed, to give C-protected L-m-sarcolysyl-L-p-fluorophenylalanine, which was then reacted with N-protected proline, to give N,C-protected L-prolyl-L-m-sarcolysyl-L-p-fluorophenylalanine. Finally the N-protecting group was removed and the HCl salt was prepd. to give Et L-prolyl-L-m-sarcolysyl-L-p-fluorophenylalanate hydrochloride in 5% yield.

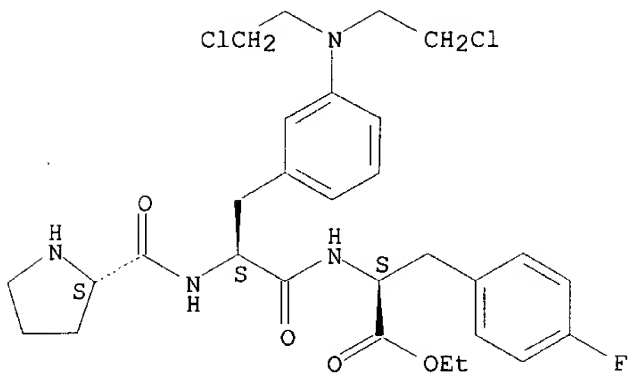
IC ICM C07K005-08
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
IT **39064-36-3P** 39256-83-2P 219859-89-9P 219859-90-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of L-prolyl-L-m-sarcolysyl-L-p-fluorophenylalanine for use as chemotherapeutic agents)
IT **35849-47-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of L-prolyl-L-m-sarcolysyl-L-p-fluorophenylalanine for use as chemotherapeutic agents)
IT **39064-36-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of L-prolyl-L-m-sarcolysyl-L-p-fluorophenylalanine for use as chemotherapeutic agents)
RN 39064-36-3 HCAPLUS
CN L-Phenylalanine, 1-[(phenylmethoxy)carbonyl]-L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **35849-47-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of L-prolyl-L-m-sarcolysyl-L-p-fluorophenylalanine for use as chemotherapeutic agents)
RN 35849-47-9 HCAPLUS
CN L-Phenylalanine, L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

REFERENCE COUNT: 3
REFERENCE(S): (1) Belfanti Ist Sieroterap Milan; BE 775775 A 1972
(2) de Barbieri, A; US 3814746 A 1974
(3) Peptichemio Ag; WO 9902177 A 1999, P6 HCAPLUS

L4 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:64700 HCAPLUS
DOCUMENT NUMBER: 130:144179
TITLE: Pharmaceutical composition containing Peptichemio for cancer treatment
INVENTOR(S): Mehlem, Francesco
PATENT ASSIGNEE(S): Peptichemio A.-G., Switz.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902177	A1	19990121	WO 1998-CH300	19980707
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9879049	A1	19990208	AU 1998-79049	19980707
EP 1001799	A1	20000524	EP 1998-929194	19980707
R: CH, DE, FR, GB, IT, LI				
JP 2001509487	T2	20010724	JP 2000-501767	19980707
EP 1132395	A2	20010912	EP 2001-201272	19980707
R: CH, DE, FR, GB, IT, LI				

PRIORITY APPLN. INFO.: CH 1997-1651 A 19970707
EP 1998-929194 A3 19980707
WO 1998-CH300 W 19980707

AB Peptichemio, a mixt. of 6 synthetic peptides each contg. L-m-sarcolysin, shows anticancer activity, esp. against melanomas. The peptides, and their lower alkyl esters and /or acid addn. salts, are formulated as

delayed-release compns. with a cyclodextrin as carrier to provide adequate bioavailability over an extended period. Thus, synthesis of 1 of the peptides, L-prolyl-L-m-sarcolysyl-L-p-fluorophenylalanine Et ester hydrochloride (I), from N-carbobenzoxy-L-proline, N-carbobenzoxy-L-m-sarcolysin, and L-p-fluorophenylalanine Et ester by the DCCD method is described. Oral cytostatic capsules contained I 12 mg and .beta.-cyclodextrin 25 g.

IC ICM A61K038-06
ICS A61K038-07; A61K038-08; A61K047-48

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 34

IT **35849-47-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compn. contg. Peptichemio for cancer treatment)

IT 32957-86-1 32976-86-6 35738-81-9 38232-13-2 38232-14-3
38232-15-4 38232-17-6 38305-84-9 39249-49-5 47812-79-3
52237-40-8 52322-24-4 214125-22-1 219859-84-4 219859-85-5
219859-86-6 219859-87-7 219859-88-8
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compn. contg. Peptichemio for cancer treatment)

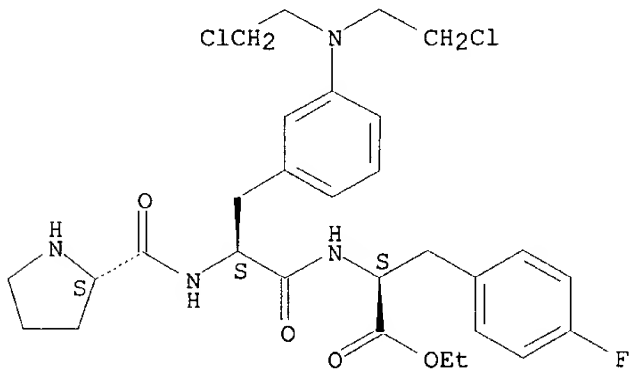
IT **39064-36-3P** 219859-89-9P 219859-90-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(pharmaceutical compn. contg. Peptichemio for cancer treatment)

IT **35849-47-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compn. contg. Peptichemio for cancer treatment)

RN 35849-47-9 HCAPLUS

CN L-Phenylalanine, L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

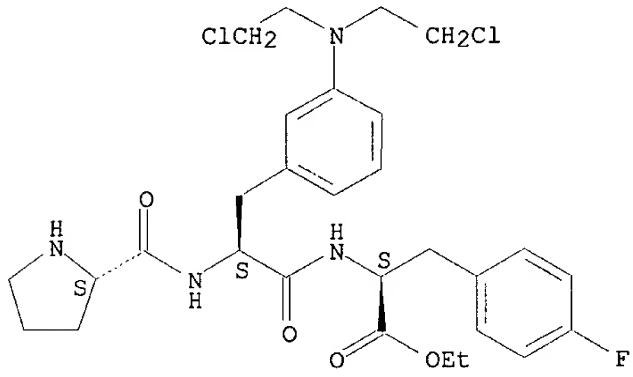
IT **52237-40-8**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compn. contg. Peptichemio for cancer treatment)

RN 52237-40-8 HCAPLUS

CN L-Phenylalanine, L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-

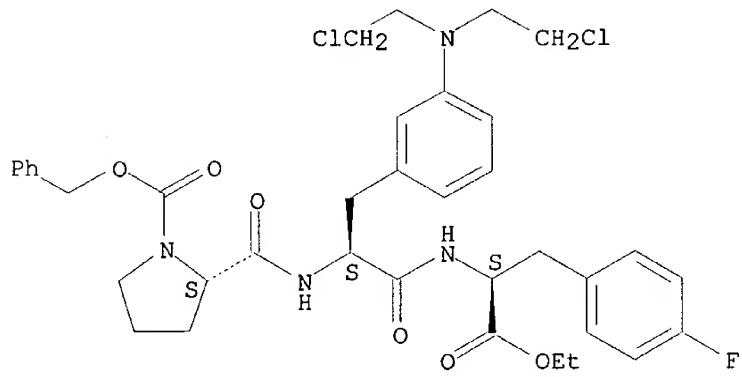
fluoro-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **39064-36-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(pharmaceutical compn. contg. Peptichemio for cancer treatment)
RN 39064-36-3 HCAPLUS
CN L-Phenylalanine, 1-[(phenylmethoxy)carbonyl]-L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5
REFERENCE(S):
(1) Astaldi; Wadley Medical Bulletin 1975, V5(3), P303 HCAPLUS
(2) Department Of The Army United States Government; WO 9420136 A 1994 HCAPLUS
(3) Istituto Sieroterapico Milanese Serafino Belfanti Ente Morale; FR 2094175 A 1972 HCAPLUS
(4) Istituto Sieroterapico Milanese Serafino Belfanti Ente Morale; FR 2101226 A 1972 HCAPLUS
(5) Rajewski; Journal of Pharmaceutical Sciences 1996, V85(11), P1142 HCAPLUS

L4 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:533040 HCAPLUS
DOCUMENT NUMBER: 129:285656
TITLE: Comparison of the cytotoxic activity of melphalan with L-prolyl-m-L-sarcolysyl-L-p-fluorophenylalanine in

human tumor cell lines and primary cultures of tumor cells from patients

AUTHOR(S): Larsson, R.; Dhar, S.; Ehrsson, H.; Nygren, P.; Lewensohn, R.

CORPORATE SOURCE: Division of Clinical Pharmacology, University Hospital, Uppsala University, Uppsala, S-75185, Swed.

SOURCE: Br. J. Cancer (1998), 78(3), 328-335
CODEN: BJCAAI; ISSN: 0007-0920

PUBLISHER: Churchill Livingstone

DOCUMENT TYPE: Journal

LANGUAGE: English

British J. of Cancer

AB M-L-sarcolysin (m-L-SL) is an isomer of melphalan (Mel) with the di(2-chloroethyl) amino group being substituted in the meta position of phenylalanine. By covalent conjugation of amino acids to m-L-SL, a peptide complex consisting of six m-L-SL-based oligopeptides known as peptichemio (PTC) was developed previously. In the present study, the cytotoxic activity pattern of the different oligopeptides of PTC was investigated in ten human tumor cell lines representing different mechanisms of cytotoxic drug resistance using the fluorometric microculture cytotoxicity assay (FMCA). In the cell line panel, L-prolyl-m-L-sarcolysyl-L-p-fluorophenylalanine (P2) was the most active oligopeptide, showing slightly lower mean IC50 values (2.6 vs 3.9 and 4.1 .mu.g ml-1) than Mel and m-L-SL. The other 5 oligopeptides were less active than Mel. All active oligopeptides showed mechanistic similarity to Mel as judged by the correlation anal. of the cell line panel log IC50 values (R .gtoreq. 0.90), although P2 appeared to be less sensitive to GSH-mediated drug resistance. The relative activity of Mel and P2 was found to be related to degree of proliferation, P2 being more active towards low-proliferating cell lines. P2 and Mel were then further characterized in 49 fresh human tumor samples. In these samples P2 was considerably more active than Mel and showed a higher relative solid tumor activity (2.7 to 4.5-fold). However, the correlation of log IC50s between P2 and Mel in patient cells was high (R = 0.79), indicating a similar mechanism of action in this tumor model too. Cross-resistance with other std. drugs was lower for P2 than Mel. The results show that P2 is the most potent component of PTC and demonstrates a favorable activity profile compared with Mel. These data suggest that further investigation of P2 as a potential anti-tumor agent is warranted.

CC 1-6 (Pharmacology)

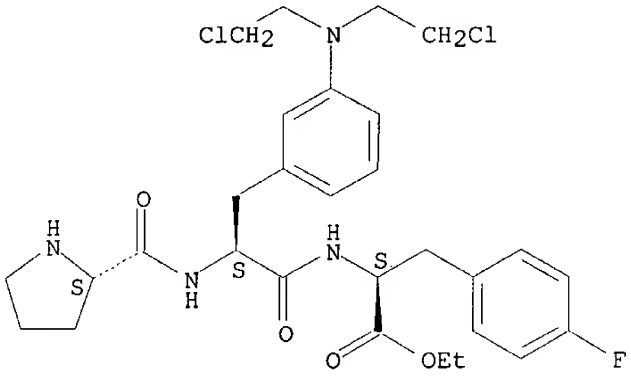
IT **52237-40-8**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(cytotoxic activity of melphalan and L-prolyl-m-L-sarcolysyl-L-p-fluorophenylalanine in tumor cell lines)

IT **52237-40-8**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(cytotoxic activity of melphalan and L-prolyl-m-L-sarcolysyl-L-p-fluorophenylalanine in tumor cell lines)

RN 52237-40-8 HCAPLUS

CN L-Phenylalanine, L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L4 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1974:458145 HCAPLUS
DOCUMENT NUMBER: 81:58145
TITLE: Antitumor chemotherapeutic action of synthetic peptides
AUTHOR(S): De Barbieri, A.; Chiappino, G.; Di Vittorio, P.; Golferini, A.; Maugeri, M.; Mistretta, A. P.; Perrone, F.; Tassi, G. C.; Temelcou, O.; Zapelli, P.
CORPORATE SOURCE: Ist. Sieroter. Milan. S. Belfanti, Milan, Italy
SOURCE: Biochim. Appl. (1972), 19(2), 29-52
CODEN: BIALAY
DOCUMENT TYPE: Journal
LANGUAGE: Italian

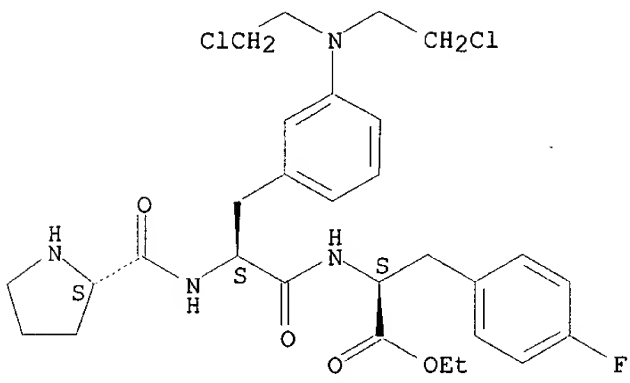
AB With the alkylating compd. m-[bis(2-chloroethyl)amino]-L-phenylalanine (I) [1088-80-8] as std., numerous synthetic compds. contg. I in peptide linkage were tested for antitumor activity in vivo and for ability to inhibit tissue enzymes in vivo. The peptides contained physiol. and (or) nonphysiol. amino acids in addn. to I. Highest activity occurred when all the amino acids were of the L-configuration. A mixt. of 6 of the most active peptides, called Peptichemio [9076-25-9], was tested extensively. Its activity against sarcoma 180 in mice was greater than that of I. Peptichemio was a potent antimitotic, slightly inhibited fertility in rats, and was devoid of teratogenicity in rats; it also had a marked antispastic effect. Structure-activity relations of the chemotherapeutic peptide are discussed with respect to the hypothesis that the constituent amino acids not only regulate the alkylating action of the I moiety but also exert an antimetabolite effect by inhibiting amino acid transport into tumor cells.

CC 1-3 (Pharmacodynamics)
IT 9076-25-9 35849-45-7 35849-52-6 35849-53-7 38232-18-7 38232-22-3 39064-52-3 52237-39-5 **52237-41-9** 52322-24-4
RL: BIOL (Biological study)
(neoplasm inhibition from)
IT **52237-41-9**
RL: BIOL (Biological study)
(neoplasm inhibition from)
RN 52237-41-9 HCAPLUS
CN L-Phenylalanine, N-[3-[bis(2-chloroethyl)amino]-N-L-prolyl-L-phenylalanyl]-4-fluoro-, ethyl ester, monoacetate (9CI) (CA INDEX NAME)

CM 1

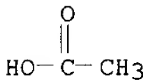
CRN 52237-40-8
CMF C29 H37 Cl2 F N4 O4

Absolute stereochemistry. Rotation (-).



CM 2

CRN 64-19-7
CMF C2 H4 O2



L4 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1973:72600 HCAPLUS
DOCUMENT NUMBER: 78:72600
TITLE: Tetracycline derivatives of synthetic m-[bis(2-chloroethyl)amino]-L-phenylalanine-containing oligopeptides
INVENTOR(S): De Barbieri, Augusto
PATENT ASSIGNEE(S): Istituto Sieroterapico Serafino Belfanti
SOURCE: Ger. Offen., 37 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2128623	A1	19730104	DE 1971-2128623	19710609

AB [In this abstr. FPhe = p-fluoro-L-phenylalanyl, ClPhe = m-[bis(2-chloroethyl)amino]-L-phenylalanyl, EtAsp = .beta.-ethyl-L-aspartyl.] The title compds. (I; R = FPhe-ClPhe-Asn-OEt, Pro-ClPhe-FPhe-OEt, Pro-ClPhe-Nva-OEt, Ser-FPhe-ClPhe-OEt, FPhe-EtAsp-ClPhe-OEt, FPhe-Gly-ClPhe-Nva-OEt) were prepd. by treating tetracycline with H2CO and the corresponding peptide. I caused Sarcoma 180 tumor regression.

IC C07C; A61K

CC 34-3 (Synthesis of Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 63

IT 32976-86-6P 35738-83-1P 35738-84-2P 35738-85-3P 35738-88-6P
35738-90-0P 35739-05-0P 35739-06-1P 35739-07-2P 35849-45-7P
35849-47-9P 35849-48-0P 35849-52-6P 35849-55-9P
39063-97-3P 39064-05-6P **39064-35-2P 39064-36-3P**

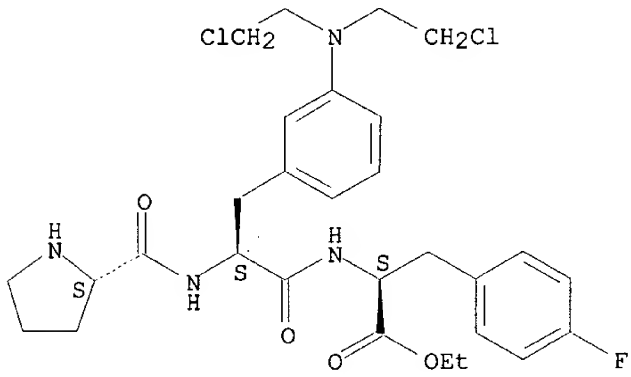
39064-51-2P 39064-52-3P 39249-46-2P 39249-49-5P 39256-65-0P
39256-77-4P 39256-78-5P 39256-79-6P 39256-80-9P 39256-84-3P
39481-37-3P 39481-38-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT **35849-47-9P 39064-35-2P 39064-36-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 35849-47-9 HCAPLUS

CN L-Phenylalanine, L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

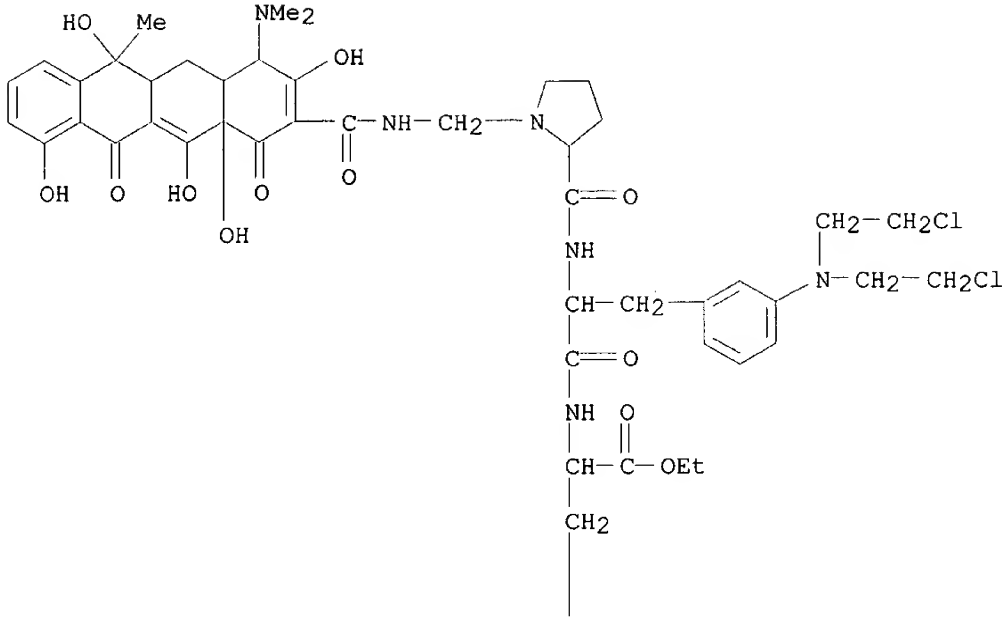


● HCl

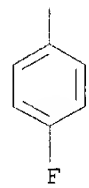
RN 39064-35-2 HCAPLUS

CN L-Phenylalanine, N-[3-[bis(2-chloroethyl)amino]-N-[1-[[[[4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenyl]carbonyl]amino]methyl]-L-prolyl]-L-phenylalanyl]-4-fluoro-, ethyl ester, monohydrochloride, [4S-(4.alpha.,4a.alpha.,5a.alpha.,6.beta.,12a.alpha.)]- (9CI) (CA INDEX NAME)

PAGE 1-A



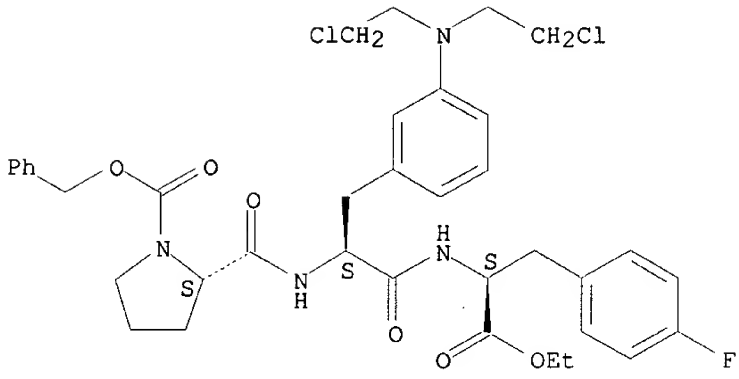
PAGE 2-A



● HCl

RN 39064-36-3 HCAPLUS
CN L-Phenylalanine, 1-[(phenylmethoxy)carbonyl]-L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



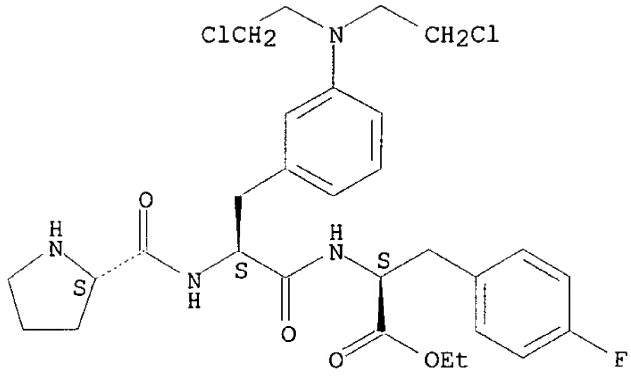
L4 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1973:30201 HCAPLUS
DOCUMENT NUMBER: 78:30201
TITLE: Tetracycline-containing peptides with antitumor activity
PATENT ASSIGNEE(S): Istituto Sieroterapico Milanese "Serafino Belfanti" Ente Morale
SOURCE: Fr. Demande, 28 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2101226		19720505		
PRIORITY APPLN. INFO.:			IT 1970-28334	19700805

AB Tetracycline derivs. (I) in which R is a di-, tri, or tetrapeptide contg. the m-[bis(2-chloroethyl)amino]phenylalanine residue were prepd. by the Mannich reaction of tetracycline with the appropriate peptide. The necessary peptides were prepd. by the dicyclohexylcarbodiimide procedure.

IC A61K; C07C
CC 34-3 (Synthesis of Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
IT 34260-39-4P 34260-42-9P 35738-86-4P 35738-88-6P 35738-90-0P
35739-05-0P 35739-06-1P 35739-07-2P **35849-47-9P**
35849-49-1P 35849-52-6P 35849-55-9P 39063-97-3P 39064-02-3P
39064-05-6P **39064-35-2P 39064-36-3P** 39064-38-5P
39064-42-1P 39064-43-2P 39064-44-3P 39064-46-5P 39064-50-1P
39064-51-2P 39064-52-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT **35849-47-9P 39064-35-2P 39064-36-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 35849-47-9 HCAPLUS
CN L-Phenylalanine, L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

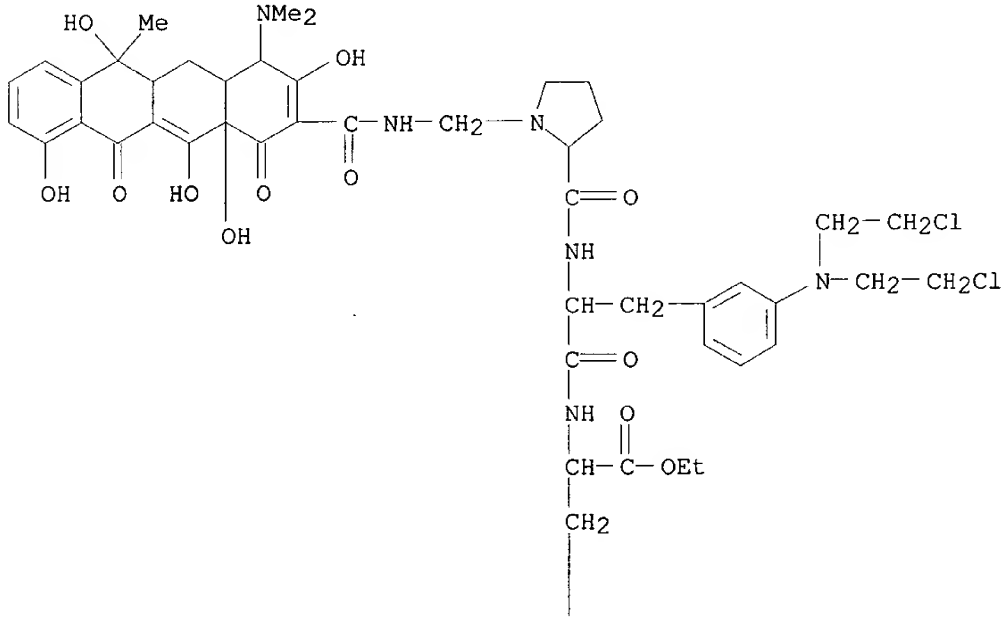
Absolute stereochemistry. Rotation (-).

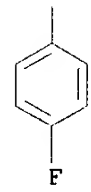


● HCl

RN 39064-35-2 HCAPLUS
CN L-Phenylalanine, N-[3-[bis(2-chloroethyl)amino]-N-[1-[[[[4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenyl]carbonyl]amino]methyl]-L-prolyl]-L-phenylalanyl]-4-fluoro-, ethyl ester, monohydrochloride, [4S-(4.alpha.,4a.alpha.,5a.alpha.,6.beta.,12a.alpha.)]- (9CI) (CA INDEX NAME)

PAGE 1-A

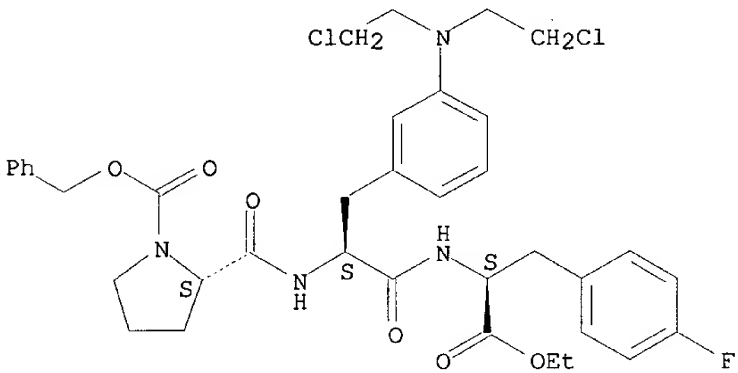




● HCl

RN 39064-36-3 HCAPLUS
CN L-Phenylalanine, 1-[(phenylmethoxy)carbonyl]-L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L4 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1972:86148 HCAPLUS
DOCUMENT NUMBER: 76:86148
TITLE: Cytostatic m-[bis(2-chloroethyl)amino]-L-phenylalanine-containing oligopeptides
INVENTOR(S): De Barbieri, Agusto
PATENT ASSIGNEE(S): Istituto Sieroterapico Serafino Belfanti
SOURCE: Ger. Offen., 53 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2128549	A	19720113	DE 1971-2128549	19710609
DE 2128549	B2	19760129		
DE 2128549	C3	19760909		
FR 2094175	A1	19720204	FR 1970-29723	19700812
FR 2094175	A5	19720204		

PRIORITY APPLN. INFO.: US 1970-45585 19700611
AB (Y = -HNCH[CH2C6H4N(CH2CH2Cl)2]CO-; -QPhe- = -HNCH-(CH2C6H4F-p)CO-; NArg = N.omega.-nitro-L-arginyl; Z = PhCH2O2C). The title compds. [I; R = H,

H-QPhe; Pro; Ser-QPhe, H-QPhe-(EtO)Asp, or HCO-QPhe; R1 = Asp-OEt, OEt, QPhe-OEt, Nva-OEt, Lys-OEt, Lys-Nva-OEt, Lys-QPhe-OEt, N-Arg-Nva-OEt, NArg-QPhe-OEt, or Arg-Lys-QPhe-His-OH] were prepd. and used as cytostatics according to Cancer Chemotherapy National Service Center methods esp. against Sarcoma 180 and Adenocarcinoma 755 in mice and addnl. clinically against several tumors. Thus, Z-Asp-OEt was hydrogenated over Pd/C in MeOH-AcOH, HCl added, the base released in DMF, and ZyOH and dicylohexylcarbodiimide added to 0.degree. to give 79% ZYAsp-OEt. The Z group was removed by hydrogenolysis in MeOH-HCl in the presence of Pd/C to give 75% I.HCl (R = H, R1 = Asp-OEt). Similarly prepd. and used were 16 other I.

IC C07C; A61K

CC 34 (Synthesis of Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 63

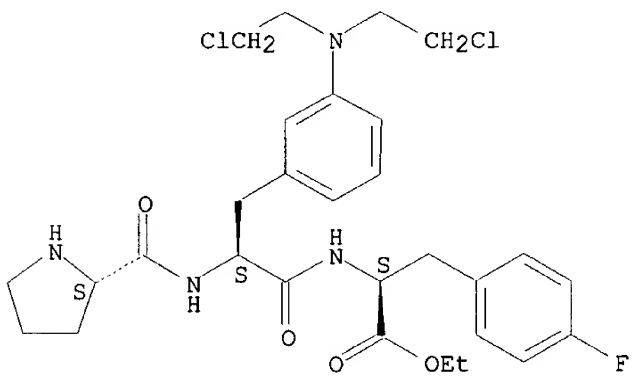
IT 32976-86-6P 35738-81-9P 35738-82-0P 35738-83-1P 35738-84-2P
35738-85-3P 35738-86-4P 35738-87-5P 35738-88-6P 35738-89-7P
35738-90-0P 35738-91-1P 35738-92-2P 35738-93-3P 35739-04-9P
35739-05-0P 35739-06-1P 35739-07-2P 35778-61-1P 35778-62-2P
35849-44-6P 35849-45-7P 35849-46-8P **35849-47-9P**
35849-48-0P 35849-49-1P 35849-50-4P 35849-51-5P 35849-52-6P
35849-53-7P 35849-54-8P 35849-55-9P 35864-84-7P 35960-30-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT **35849-47-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 35849-47-9 HCAPLUS

CN L-Phenylalanine, L-prolyl-3-[bis(2-chloroethyl)amino]-L-phenylalanyl-4-fluoro-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl